

**Notice of Allowability**

Application No.

10/563,193

Applicant(s)

NEYSES, LUDWIG

Examiner

SAMIRA JEAN-LOUIS

Art Unit

1627

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 02/11/2011.
2. ☒ The allowed claim(s) is/are 23-25 and 27-29 (renumbered 1-6).
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- \* Certified copies not received: \_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |  |  |
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| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)   | 5. <input type="checkbox"/> Notice of Informal Patent Application  |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date <u>04/19/11</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date ____     | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment  |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance                         |
|  | 9. <input type="checkbox"/> Other ____.  |

## **DETAILED ACTION**

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in an e-mail communication with Alan Heimlich on April 20<sup>th</sup>, 2011.

The application has been amended as follows:

1. In claim 24, line 11, after "is diagnostic of infertility" insert "; and counting a number of non-motile sperm cells relative to motile sperm cells in the biological sample, wherein a number of non-motile sperm cells is greater than 30%".
2. Cancel claims 14-22.

### **EXAMINER'S STATEMENT OF REASONS FOR ALLOWANCE**

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Applicant's amendment to the claims filed February 11<sup>th</sup>, 2011 has been fully considered. In light of Applicant's amendment and the Examiner's amendment, claims 23-25 and 27-29 are allowed and renumbered to claims 1-6.

In light of the cancellation of claims 14-22, the 102 (b) rejection of claim 20 over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030) is withdrawn.

In light of the cancellation of claims 14-22, the 103 (a) rejection of claim 21 over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030) in view of Pasquale (U.S. 4,066,757) is withdrawn.

In light of the cancellation of claims 14-22, the 112, second paragraph rejection of claim 22 is hereby withdrawn.

In light of the cancellation of claims 14-22, the 103 (a) rejections of claims 14-15 and 17-19 over Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030) in view of Wennemuth et al. (J. Gen. Physiol. June 30, 2003, Vol. 122, pgs. 115-128); of claim 16 in further view of Zimmerman et al. (U.S. 2002/0164368); of claim 23 in further view of Perloe et al. (The formula of Male Fertility, Published online

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February 2002, pgs. 1-9); and of claim 25 in further view of (Burnett et al. (Toxicology, 1997, Vol. 119, pgs. 83-93) are withdrawn.

The following is an examiner's statement of reasons for allowance: Claims 23-25 and 27-29 are drawn to a method for diagnosing infertility in a human male, comprising: obtaining a biological sample from the human male, wherein the biological sample contains one or more cells; analyzing the biological sample, wherein (i) detecting a mutation or polymorphism in a plasma membrane calcium ATPase 4 (PMCA4) gene encoding PMCA4 in the one or more sperm cells, or (ii) detecting a decrease in the expression of PMCA4 in the one or more sperm cells relative to a control sample, is diagnostic of infertility; and counting a number of non-motile sperm cells relative to motile sperm cells in the biological sample, wherein a number of non-motile sperm cells is greater than 30%. There is no prior art disclosing applicant's diagnostic method of treatment, particularly detecting a mutation in the PMCA4 gene as disclosed in claim 23. The closest art Chaudhary et al. (Am. J. Physiol Cell Physiol. 2001, Vol. 280, pgs. C1027-C1030) in view of Wennemuth et al. (J. Gen. Physiol. June 30, 2003, Vol. 122, pgs. 115-128). Chaudhary et al. teach that the PM  $\text{Ca}^{2+}$  pumps are present in all mammalian cells (i.e. inclusive of sperm cells) thereby suggesting that such pumps are also present in humans as well (see pg. C1027, left col., Introduction Section and pg. C1029, right col., last col.). Chaudhary et al. further teach that Caloxin 2A1 was able to bind PMACA1 and produced a complete inhibition of PM  $\text{Ca}^{2+}$  pumps in erythrocytes that mainly express PMCA4 (see pg. C1029, left col., Discussion Section, paragraph 4) thus suggesting that Caloxin 2A1 could be used for inhibiting PMCA4 since PMAC1 and

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PMCA4's sequences are similar. Chaudhary et al. do not specifically teach a method for diagnosing infertility in a human male as recited in claim 23. Wennemuth teaches that past studies show that  $\text{Ca}^{2+}$  signals produced by the opening of PM membrane channels initiate several events required for the sperm to reach and enter the egg but reveal little about how resting  $\text{Ca}^{2+}$  is maintained or restored after elevation (see abstract). However, Wennemuth also teaches that PMCA and NCX  $\text{Ca}^{2+}$  pumps work in synergy to clear  $\text{Ca}^{2+}$ . Thus, one skilled in the art would have been unable to attribute a particular pump to the functioning of sperm cell. Moreover, applicant is the first to correlate the specific physiological significance of PMCA for sperm function (see specs., pg. 5, lines 23-29). Since the present claims require detection of mutation or polymorphism in PMCA4 gene or detection of decreased expression of PMCA4 protein in sperm cells in the aforementioned diagnostic method, and Chaudhary et al. alone do not render obvious the particular diagnostic method of claim 23, claims 23-25 and 27-29 are therefore allowable.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### ***Conclusion***

Claims 23-25 and 27-29 (renumbered 1-6) are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

04/23/2011

/SREENI PADMANABHAN/

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Supervisory Patent Examiner, Art Unit 1627